

## Nontechnical Abstract

ADA Deficiency is a fatal genetic disease that often results in death within the first years of life. The disease is characterized by a loss of immune cells (the lymphocytes) in the body and this results in a profound immunodeficiency, called Severe Combined Immunodeficiency (SCID). The disease is caused by a defect in one of the genes that is required for the proper functioning of the T lymphocytes. The treatment of choice is a matched bone marrow transplantation. But for those patients who are not candidates for bone marrow transplantation, we propose to attempt to provide immune protection by using gene therapy. The procedure would be to remove T lymphocytes from patients who are on PEG-ADA, grow the T cells in tissue culture, insert a normal ADA gene into them using a process called retroviral-mediated gene transfer, and then return the gene-corrected cells to the patient.

The protocol is designed to have two parts. In Part 1, low numbers of gene-corrected T lymphocytes would be given to the patient repeatedly in order to build up the immune system and also to obtain information as to how long gene-corrected T cells survive. In Part 2A, a selection procedure would be used to increase the number of gene-corrected T cells making substantial amounts of the ADA enzyme. These enriched cells would then be given to the patient monthly for approximately six months. In Part 2B, the number of gene-corrected T cells would be escalated to the predicted therapeutic level (probably around 1 billion gene-corrected T cells per kilogram body weight of the patient). Then, 1 to 3 billion gene-corrected T cells per kg would be infused several times and the patient would be monitored in order to determine if significant clinical improvement has occurred.